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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/413,110 | 10/06/1999 | EVAN C. UNGER | UNGR-1580 | 1596 |

7590 12/26/2001

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EXAMINER

SHARAREH, SHAHNAM J

| | |
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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1619

DATE MAILED: 12/26/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/413,110

Applicant(s)

UNGER, EVAN C.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 116-184 is/are pending in the application.
- 4a) Of the above claim(s) 132-137, 142-145, 152-159, 161-163, 167 and 175-177 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 116-131, 138-141, 146-151, 160, 164-166, 168-174 and 178-184 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s)-filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 20.

- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

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PTO-326 (Rev. 04-01)

Office Action Summary

Part of Paper No. 22

DETAILED ACTION

Amendment filed on October 05, 2001 have been entered. Claim 116-184 are pending.

Response to Amendment

Any of the previously made rejection that is not addressed in this Office Action is considered obviated in view of the Amendments.

Status of the Claims

For clarification purposes, Examiner states that the restriction requirement as set forth in Paper No. 4 was proper, as the restricted groups were directed to two distinct methods related as combination and subcombination for the reasons of record. Further, Examiner acknowledges that the instant claims are directed to methods of enhancing delivery of a bioactive agent comprising (i) administering an agent to a patient, (ii) administering a vesicle composition comprising an aqueous carrier, a gas or gaseous precursor, and vesicles comprising lipids, proteins or polymers to the patient (iii) and applying ultrasonic energy to a tissue to cause cavitations or rupture of said vesicles, wherein the gas comprise a perfluorocarbon, and the tissue is a reduced perfusion tissue. Accordingly, as the instant claims are directed to methods of drug delivery to reduced perfusion tissues, they encompass such tissues affected by vascular thrombosis.

This Application contains claims 132-137, 142-145, 152-159, 161-163, 167, 175-177 drawn to nonelected species. A complete reply to the final rejection must include

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cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed September 26, 2001 have been fully considered but they are not persuasive.

Claims 116-131, 138-141, 146-151, 160,164, 168-174, and 178-184 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over patented claims of U.S. Patent No. 6,143,276 ^{and} 5,580,575.

The conflicting claims are not patentably distinct from each for the reasons of record. Both sets of claims are still directed to methods of delivering a bioactive agent in combination with a gaseous liposomal composition and then applying an ultrasonic energy source. However, the rejection of claims over US Patents 6,123,923 and 5,770,222 has been withdrawn.

Claims 116-131, 138-141, 146-151, 160,164, 168-174, and 178-184 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the pending claims of copending Application No. 09/218,660. the conflicting claims are still not patentably distinct from each other for the reasons of record.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Examiner notes Applicant's intention to file a terminal disclaimer once a favorable ruling is issued.

Claims 116-131, 138-140, 160, 164-166, 168-174, and 178-184 stand rejected under 35 U.S.C. 102(b) as being anticipated by Siegel US Patent 5,695,460.

Applicant's arguments that the instant claims are directed to methods of delivery of the bioactive agent out of the vasculature and into the selected tissue or to an extravascular tissue, is not commensurate with the scope of the pending claims, as the claims are not directed to such limitations.

Further, the recitation that an element is "sufficient" or "capable" to perform a given function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchinson*, 69 USPQ 138. Accordingly, as the process steps of Siegel are the same as the instantly claimed methods, and the instantly claimed tissue encompasses vascular ischemic tissues; Siegel's delivery of thrombolytics to vascular-ischemic tissues anticipates the limitations of the instant claims.

Moreover, in response to applicant's argument that Siegel's method is directed to a different purpose, Examiner replies that the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In the instant case, the process steps of Siegel are the same as the instantly claimed methods. Thus, Siegel anticipates the limitations of the instant claims.

Claims 141, 146-151 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al US Patent 5,695,460.

Applicant argues that the instant methods are directed to delivering a bioactive agent, and Siegel's methods are directed to a different purpose. In reply Examiner states that as discussed above, Siegel clearly teaches the method steps of the instant claims, accordingly, modifying the rate of infusion would have been achieved by routine experimentation.

Claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, and 178-184 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Porter US Patent 5,648,098 in view of Siegel et al US Patent 5,695,460.

Applicant argues that neither of the cited references is directed to delivery of a bioactive agent. In response Examiner states that Porter specifically sets forth delivery of medicaments other than thrombolytic agents to the site of thrombosis (see col 10, lines 20-25). Porter also indicates that such medicaments may be a radiographic dye (see col 8, lin 15-16). Thus, Porter provides for the general delivery of medicaments to a site of interest. Siegel teaches delivery of thrombolytics to a thrombus. Accordingly, as suggested in previous Office Action, the combined teachings of Porter and Siegel render the instant methods of delivery obvious.


Conclusion

No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is (703) 306-5400. The examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana Dudash can be reached on 703-308-2328. The fax phone number for this Group is 703-308-4556. Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 703-308-1235.

sjs 12/12/01



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